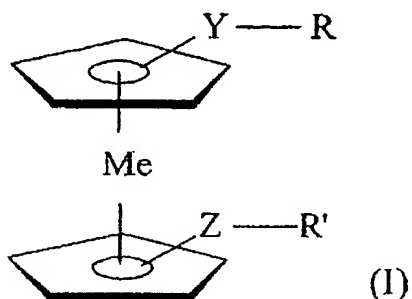


WHAT IS CLAIMED IS

1. A bifunctionalized metallocene of general formula (I):

5



in which

- Me represents a transition metal, preferably chosen from Fe, Ru and Os,
  - Y and Z, which are identical, are chosen from  $-(CH_2)_n-O-$ ,  $-(CH_2)-O-[(CH_2)_2-O]_p-$  and  $-(CH_2)_q-CONH-(CH_2)_r-O-$ , or else
  - Y is  $-(CH_2)_s-NH-$  and Z is  $-(CH_2)_t-COO-$ ,
  - n is an integer between 3 and 6,
  - p is an integer between 1 and 4,
  - q is an integer between 0 and 2,
  - r is an integer between 0 and 2,
  - s is an integer between 2 and 5,
  - t is an integer between 3 and 6,
  - R and R' represent hydrogen atoms or are protective groups used in the synthesis of oligonucleotides and peptides, it being understood that at least one of R or R' is a protective group used in the synthesis of oligonucleotides and peptides and that R and R' are as defined below:
- (i) when Z and Y are chosen from  $-(CH_2)_n-O-$ ,  $-(CH_2)-O-[(CH_2)_2-O]_p-$  and  $-(CH_2)_q-CONH-(CH_2)_r-O-$ , then R and R' are protective groups used in the synthesis of oligonucleotides, and R is a group capable of leaving a free hydroxyl group after deprotection, preferably a photolabile group, monomethoxytrityl, dimethoxytrityl, tert-

butyldimethylsilyl, acetyl or trifluoroacetyl, and R' is a phosphorus group capable of reacting with a free hydroxyl group, preferably a phosphodiester, phosphoramidite or H-phosphonate group, and

5

(ii) when Y is  $-(CH_2)_s-NH-$  and Z is  $-(CH_2)_t-COO-$ , then R is a protective group used in the synthesis of peptides and represents a protective group for amines, preferably 9-fluorenyloxycarbonyl, tert-butoxycarbonyl or benzyloxycarbonyl, and R' represents a hydrogen atom.

10

15

2. The metallocene as claimed in claim 1, characterized in that Me is iron.

20

3. The metallocene as claimed in either of claims 1 and 2, characterized in that Y and Z are chosen from  $-(CH_2)_n-O-$ ,  $-(CH_2-O-[(CH_2)_2-O]_p-$  and  $-(CH_2)_q-CONH-(CH_2)_r-O-$ .

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4. The metallocene as claimed in one of claims 1 to 3, characterized in that Y and Z are each  $-(CH_2)_n-O-$ , n being equal to 3.

5. The metallocene as claimed in one of claims 1 to 3, characterized in that Y and Z are each  $-(CH_2)-O-[(CH_2)_2-O]_p-$ , p being equal to 2.

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6. The metallocene as claimed in either of claims 1 and 2, characterized in that Y is  $-(CH_2)_s-NH-$ , Z is  $-(CH_2)_t-COO-$ .

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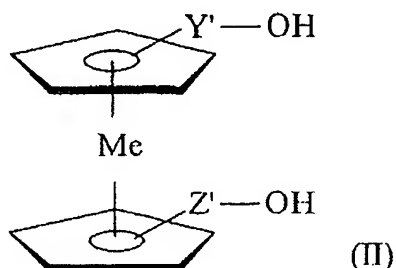
7. The metallocene as claimed in claim 6, characterized in that s is equal to 3 and t is equal to 4.

8. A process for the preparation of a metallocene of formula (I) as claimed in any one of claims 3 to

5, characterized in that it comprises the following stages:

- a stage of protection of one of the hydroxyl groups of a compound of general formula (II):

5



in which Me is as defined in the preceding claims, Y' and Z', which are identical, are chosen from  
 10  $-(CH_2)_n-$ ,  $-(CH_2)-O-[(CH_2)_2-O]_{p'}-(CH_2)_2-$  and  $-(CH_2)_q-CONH-(CH_2)_r-$ , n, q and r are as defined in the preceding claims and p' is an integer between 0 and 3,

by attachment of a group capable of leaving a free hydroxyl group after deprotection, preferably  
 15 chosen from a photolabile group, monomethoxytrityl, dimethoxytrityl, tert-butyldimethylsilyl, acetyl and trifluoroacetyl, and

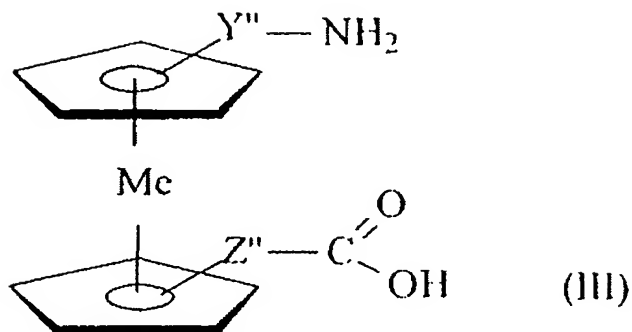
20 - a stage of coupling, to the other hydroxyl group left free, a phosphorus group capable of reacting with a free hydroxyl group, preferably chosen from the phosphodiester, phosphoramidite and H-phosphonate groups.

25

9. A process for the preparation of a metallocene of formula (I) as claimed in either of claims 6 and 7, characterized in that it comprises the following stages:

30

- a stage of protection of the  $NH_2$  group of a compound of general formula (III):

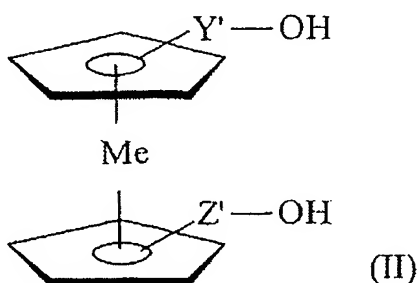


in which

- Me is as defined in either of above claims,
- 5    - Y' ' is  $-(CH_2)_s-$  and
- Z' ' is  $-(CH_2)_t-$ ,
- s and t being as defined in either of above claims,

by attachment of a group capable of leaving a free  
 10    amine functional group after deprotection,  
      preferably chosen from 9-fluorenyloxycarbonyl,  
      tert-butoxycarbonyl and benzyloxycarbonyl.

10. A bis(hydroxy)metallocene of general formula (II):
- 15



in which

- Me is a transition metal, preferably chosen from Fe, Ru and Os,
- 20    - Y' and Z', which are identical, are chosen from  $-(CH_2)_n-$ ,  $-(CH_2)-O-[(CH_2)_2-O]_{p'}-(CH_2)_2-$  and  $-(CH_2)_q-CONH-(CH_2)_r-$ ,
- n is an integer between 3 and 6,
- p' is an integer between 0 and 3,
- 25    - q is an integer between 0 and 2, and
- r is an integer between 0 and 2,

it being understood that, when Me is Fe or Ru and when Y' and Z' are  $-(CH_2)_n-$ , then n is 5 and, when Me is Fe and when Y' and Z' are  $-(CH_2)-O-[(CH_2)_2-O]_{p'}-(CH_2)-$ , then p' is 0.

- 5
11. The bis(hydroxy)metallocene as claimed in claim 10, characterized in that Me is iron.
12. The bis(hydroxy)metallocene as claimed in claim 10, characterized in that Y' and Z' are each  $-(CH_2)_n-$ , n being equal to 3.
13. The bis(hydroxy)metallocene as claimed in either of claims 10 and 11, characterized in that Y' and Z' are each  $-(CH_2)-O-[(CH_2)_2-O]_{p'}-(CH_2)-$ , p' being equal to 0.
14. A process for labeling an oligonucleotide with a bifunctionalized metallocene of formula (I) as claimed in any one of claims 3 to 5, characterized in that it comprises the substitution of one or more nucleotide synthons by one or more of said metallocenes of formula (I), in which R and R' are protective groups used in the synthesis of oligonucleotides, in the cycle for the synthesis of said oligonucleotide.
15. The process as claimed in claim 14, characterized in that the substitution is carried out in the 3'- or 5'-positions in replacement of the first or last nucleotides, respectively.
16. A process for labeling a peptide by a bifunctionalized metallocene of formula (I) as claimed in either of claims 6 and 7, characterized in that it comprises the substitution of one or more amino acid synthons by one or more of said metallocenes of formula (I), in which R represents a protective group for amines and R' represents a

hydrogen atom, in the cycle for the synthesis of said peptide.

17. The process as claimed in claim 16, characterized  
5 in that the substitution is carried out at the C-terminal or N-terminal ends in replacement of the first or last amino acids, respectively.
18. The process as claimed in any one of claims 14 to  
10 17, characterized in that at least two consecutive substitutions are carried out.
19. A labeled oligonucleotide, characterized in that  
15 it is capable of being obtained by the labeling process as claimed in either of claims 14 and 15.
20. A labeled oligonucleotide, characterized in that  
at least one of the nucleosides constituting it is  
substituted by a bis(hydroxy)metallocene of  
20 general formula (II) as claimed in one of claims 10 to 13.
21. The labeled oligonucleotide as claimed in either  
of claims 19 and 20, characterized in that it  
25 comprises at least one of bis(hydroxy)metallocene of general formula (I) in the 3'- or 5'-position.
22. A labeled peptide, characterized in that it is  
capable of being obtained by the process as  
30 claimed in any one of claims 16 to 18.
23. A labeled peptide, characterized in that at least  
one of the amino-acids constituting it is  
substituted by a bifunctionalized metallocene of  
35 formula (III) as defined in claim 9.
24. The peptide as claimed in either of claims 22 and  
23, characterized in that it comprises at least

one bifunctionalized metallocene of formula (III) at the C-terminal or N-terminal ends.

- 5      25. A support for the synthesis of oligonucleotides, characterized in that at least one metallocene of formula (I) as claimed in one of claims 1 to 7 is grafted to said support by covalent reaction of one of its functionalized ends.